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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,647	POOLE, A. ROBIN	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006 and 31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments, remarks, and substitute sequence listing are acknowledged. The substitute sequence listing has been entered.

2. Claims 1-51 have been canceled.

Claims 52-61 have been added and are being acted upon.

3. In view of the cancellation of all previous claims, all previous rejections have been withdrawn. Relevant arguments will be addressed where appropriate.

4. The following are new grounds for rejection necessitated by Applicant's amendment.

5. Claims 60 and 61 are objected to as neither ends with a period.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 52-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. More specifically, the specification provides insufficient evidence that the method of the instant claims would function as claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the

quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

A review of the specification discloses that the method of the instant claims presumably functions to measure the progression (or for the monitoring) of OA or RA through a measurement of C1,2C/C2C or C2C/C1,2C ratios, wherein a higher C1,2C/C2C indicates the progression of OA and a lower C1,2C/C2C ratio indicates the progression of RA. Two brief examples are offered in support of the claimed method.

First note that the newly amended claims fail to recite how the claimed method is to be used. The claims simply recite the measurement of C1,2C epitope to C2C epitope ratios. Said measurement alone has no use. In light of the instant specification said measurement would have value only for monitoring or predicting OA or RA, and then only when the measured values are compared to some standard. Thus, the claims, e.g., 52 and 56, are incomplete and are not enabled. Also, the specification itself discloses that the claimed method does not function in RA patients with "early disease presentation". For these reasons alone the claimed method must be considered to be unpredictable and requiring of undue experimentation. A review of the examples shows that their disclosures must be further questioned. Note that neither

example actually discloses any data. Only conclusions are reported. Absent the data used to establish the reported conclusions, the value of said results cannot be established. Also note that in Example 1, "Knees with the highest grade at baseline were excluded". The selective choosing of data points for inclusion in results is not generally considered to result in scientifically credible conclusions.

A review of the relevant art also shows that in contrast to what the claims might predict, an increase in C2C is generally considered to indicate the progression of OA. See, for example, Poole (2003, IDS, Applicant's own work). At page 811 the reference teaches that an increase in C2C accompanies the induction of OA. See also Chu et al. (2002, of record), Figure 1, which teaches similar findings. Regarding RA, see Verstappen et al. (2006, of record), page 5, column 2, wherein it is taught that RA progression is accompanied by increases in both C2C and C1,2C. Also note that Poole (2003) teaches that a number of considerations "confound" the use of biomarkers for the measure of arthritis. Said marker considerations include biomarker concentrations, which vary from tissue to joint, to serum, biomarker half-life, patient age and sex, and even circadian rhythms; none of these considerations are disclosed in the instant specification. Accordingly, the method of the instant claims must be considered unpredictable and requiring of undue experimentation.

Applicant's arguments, filed 8/07/06 in response to the previous rejections, have been fully considered but they are not persuasive. Applicant argues that Claims 52 and 53 are drawn to a method for predicting progression of non-generalized osteoarthritis and osteoarthritis of the knee and that Example 2 provides significant correlation for the assay at Visit 2 with the clinical changes from Visit 2 to Visit 3.

As set forth in the rejection, the minimal disclosure of the specification is insufficient to support the claimed method. Regarding non-generalized osteoarthritis and osteoarthritis of the knee, Applicant's own post-filing work casts doubt on the claimed method. Regarding RA, as set forth in the rejection, the claimed method does not function in RA patients with "early disease presentation" and these patients have not been excluded from the claimed method. Further, see Verstappen et al. (2006, of record) and Poole (2003, IDS) for additional reasons supporting the lack of enablement.

8. Claims 52-61 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) A method of detecting relative cleavage of type I collagen … (Claim 52).

B) … non-generalized OA … (Claim 53).

C) The method of Claim 56.

Regarding A), the specification at page 6 discloses only that the cleavage products of type I collagen are minor serum biomarkers. Said markers are not disclosed as being employed in the claimed method.

Regarding B), the term is not found in the specification.

Regarding C), the specification does not disclose a method comprising the specific steps recited in the claim.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 52-61 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step indicating what the determination of the C1,2C/C2C or C2C/C1,2C ratio indicates, and in particular what the ratios are compared to. The claims simply recite the detecting of collagen cleavage. It is clear from the specification that said determination alone would be meaningless. It is the comparison of the differences in ratios of an OA or RA patient's cleavage products to some control or

standard that assertedly is used to determine the progression of disease.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

14. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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6/19/07